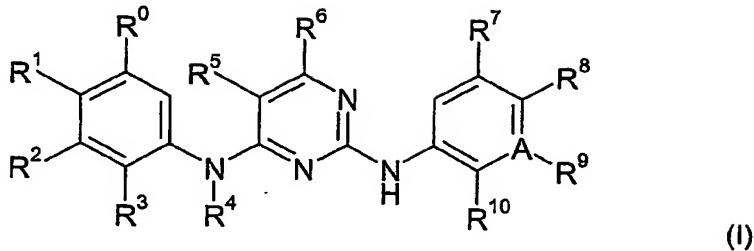


Claims

1. A compound of formula I



wherein

each of R⁰, R¹, R², and R³ independently is hydrogen, C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkinyl, C₃-C₈cycloalkyl, C₃-C₈cycloalkylC₁-C₈alkyl, C₅-C₁₀arylC₁-C₈alkyl, hydroxyC₁-C₈alkyl, C₁-C₈alkoxyC₁-C₈alkyl, aminoC₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted C₅-C₁₀aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1, 2 or 3 hetero atoms selected from N, O and S, hydroxy, C₁-C₈alkoxy, hydroxyC₁-C₈alkoxy, C₁-C₈alkoxyC₁-C₈alkoxy, haloC₁-C₈alkoxy, unsubstituted or substituted C₅-C₁₀arylC₁-C₈alkoxy, unsubstituted or substituted heterocycloloxy, or unsubstituted or substituted heterocyclylC₁-C₈alkoxy, unsubstitued or substituted amino, C₁-C₈alkylthio, C₁-C₈alkylsulfinyl, C₁-C₈alkylsulfonyl, C₅-C₁₀arylsulfonyl, halogen, carboxy, C₁-C₈alkoxycarbonyl, unsubstitued or substituted carbamoyl, unsubstitued or substituted sulfamoyl, cyano or nitro; or R⁰ and R¹, R¹ and R², and/or R² and R³ form, together with the carbon atoms to which they are attached, a 5 or 6 membered carbocyclic or heterocyclic ring comprising 0, 1, 2 or 3 heteroatoms selected from N, O and S;

R⁴ is hydrogen or C₁-C₈alkyl;

each of R⁵ and R⁶ independently is hydrogen, C₁-C₈alkyl, C₁-C₈alkoxyC₁-C₈alkyl, haloC₁-C₈alkyl, C₁-C₈alkoxy, halogen, carboxy, C₁-C₈alkoxycarbonyl, unsubsttued or substituted carbamoyl, cyano, or nitro; and

each of R⁷, R⁸, R⁹, and R¹⁰ independently is C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkinyl, C₃-C₈cycloalkyl, C₃-C₈cycloalkylC₁-C₈alkyl, C₅-C₁₀arylC₁-C₈alkyl, hydroxyC₁-C₈alkyl, C₁-C₈alkoxyC₁-C₈alkyl, aminoC₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted C₅-C₁₀aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1, 2 or 3 hetero atoms selected from N, O and S, hydroxy, C₁-C₈alkoxy, hydroxyC₁-C₈alkoxy, C₁-C₈alkoxyC₁-C₈alkoxy, haloC₁-C₈alkoxy, unsubstituted or substituted C₅-C₁₀arylC₁-C₈alkoxy, unsubstituted or substituted heterocycloloxy, or unsubstituted or substituted heterocyclylC₁-

C_8 alkoxy, unsubstituted or substituted amino, C_1 - C_8 alkylthio, C_1 - C_8 alkylsulfinyl, C_1 - C_8 alkylsulfonyl, C_5 - C_{10} arylsulfonyl, halogen, carboxy, C_1 - C_8 alkoxycarbonyl, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl, cyano or nitro; wherein R^7 , R^8 and R^9 independently of each other can also be hydrogen; or R^7 and R^8 , R^8 and R^9 , and/or R^6 and R^{10} form together with the carbon atoms to which they are attached, a 5 or 6 membered carbocyclic or heterocyclic ring comprising 0, 1, 2 or 3 heteroatoms selected from N, O and S;

A is C or N;
and salts thereof.

2. A compound of formula I according to claim 1, wherein
each of R^0 or R^2 independently is hydrogen, C_1 - C_8 alkyl, hydroxy C_1 - C_8 alkyl, halo C_1 - C_8 alkyl, unsubstituted or substituted C_5 - C_{10} aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_5 - C_{10} aryloxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclyl C_1 - C_8 alkoxy, unsubstituted or substituted amino, C_1 - C_8 alkylsulfonyl, halogen, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl;
- R^1 is hydrogen, C_1 - C_8 alkyl, hydroxy C_1 - C_8 alkyl, halo C_1 - C_8 alkyl, unsubstituted or substituted C_5 - C_{10} aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_5 - C_{10} aryloxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclyl C_1 - C_8 alkoxy, unsubstituted or substituted amino, C_1 - C_8 alkylsulfonyl, halogen, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl;
- R^3 is hydrogen, C_1 - C_8 alkyl, hydroxy C_1 - C_8 alkyl, halo C_1 - C_8 alkyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 heteroatoms selected from N, O and S, C_1 - C_8 alkoxy, substituted amino, C_1 - C_8 alkylsulfonyl, C_5 - C_{10} arylsulfonyl, halogen, carboxy, substituted or unsubstituted carbamoyl, unsubstituted or substituted sulfamoyl; or each pair of adjacent substituents R^0 and R^1 , or R^1 and R^2 , or R^2 and R^3 is $-CH_2-NH-CO-$, $-CH_2-CH_2-NH-CO-$, $-CH_2-CO-NH-$, $-CH_2-CH_2-CO-NH-$, $-CH_2-NH-SO_2-$, $-CH_2-CH_2-NH-SO_2-$, $-CH_2-SO_2-NH-$, $-CH_2-CH_2-SO_2-NH-$, $-CH_2-CH_2-SO_2-$, $-CH_2-CH_2-CH_2-SO_2-$, $-O-CH_2-O-$, or $-O-CF_3-$ $O-$, and such pairs wherein hydrogen in NH is replaced by C_1 - C_8 alkyl;
- R^4 is hydrogen or C_1 - C_8 alkyl;
- R^5 is hydrogen; C_1 - C_8 alkyl, halogen, halo C_1 - C_8 alkyl, cyano or nitro;

R⁶ is hydrogen;

each of R⁷ and R⁹ independently is hydrogen, C₁-C₈alkyl, hydroxyC₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted C₅-C₁₀aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C₁-C₈alkoxy, haloC₁-C₈alkoxy, C₅-C₁₀aryloxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclylC₁-C₈alkoxy, unsubstituted or substituted amino, C₁-C₈alkylsulfonyl, halogen, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl;

R⁸ is hydrogen, C₁-C₈alkyl, hydroxyC₁-C₈alkyl, haloC₁-C₈alkyl, C₅-C₁₀aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C₁-C₈alkoxy, haloC₁-C₈alkoxy, C₅-C₁₀aryloxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclylC₁-C₈alkoxy, unsubstituted or substituted amino, C₁-C₈alkylsulfonyl, halogen, unsubstituted or substituted carbamoyl, unsubstituted or substituted sulfamoyl, cyano, or nitro; and

R¹⁰ is C₁-C₈alkyl, hydroxyC₁-C₈alkyl, haloC₁-C₈alkyl, C₁-C₈alkoxy, unsubstituted or substituted heterocyclylC₁-C₈alkoxy, unsubstituted or substituted amino, halogen, carboxy, carbamoyl, or unsubstituted or substituted sulfamoyl; or

each pair of adjacent substituents R⁷ and R⁸, or R⁸ and R⁹ or R⁹ and R¹⁰, is -NH-CH=CH-, -CH=CH-NH-, -NH-N=CH-, -CH=N-NH-, -CH₂-CH₂-CH₂-, -CH₂-CH₂-CH₂-CH₂-, -CH₂-CH₂-O-, -CH=CH-O-, -O-CH₂-O-, or -O-CF₂-O-;

A is C or N.

3. A compound of formula I according to claim 1, wherein

each of R⁰ or R² independently is hydrogen, C₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C₁-C₈alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclylC₁-C₈alkoxy, unsubstituted or substituted amino, or halogen;

R¹ is hydrogen, C₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, C₁-C₈alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclylC₁-C₈alkoxy, unsubstituted or substituted amino, halogen;

R³ is hydrogen, C₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 heteroatoms selected from N, O and S, C₁-C₈alkoxy,

substituted amino, $C_1\text{-}C_8$ alkylsulfonyl, $C_5\text{-}C_{10}$ arylsulfonyl, halogen, carboxy, substituted or unsubstituted carbamoyl, or unsubstituted or substituted sulfamoyl; or each pair of adjacent substituents R^0 and R^1 , or R^1 and R^2 , or R^2 and R^3 is $-\text{CH}_2\text{-NH-CO-}$, $-\text{CH}_2\text{-NH-SO}_2^-$, $-\text{CH}_2\text{-CH}_2\text{-SO}_2^-$, $-\text{O-CH}_2\text{-O-}$, or $-\text{O-CF}_2\text{-O-}$, and such pairs wherein hydrogen in NH is replaced by $C_1\text{-}C_8$ alkyl;

R^4 is hydrogen;

R^5 is hydrogen, halogen, halo $C_1\text{-}C_8$ alkyl, or nitro;

R^6 is hydrogen;

each of R^7 and R^8 independently is hydrogen, $C_1\text{-}C_8$ alkyl, halo $C_1\text{-}C_8$ alkyl, unsubstituted or substituted $C_5\text{-}C_{10}$ aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, $C_1\text{-}C_8$ alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclyl $C_1\text{-}C_8$ alkoxy, unsubstituted or substituted amino, halogen, unsubstituted or substituted carbamoyl, or unsubstituted or substituted sulfamoyl;

R^8 is hydrogen, $C_1\text{-}C_8$ alkyl, halo $C_1\text{-}C_8$ alkyl, $C_5\text{-}C_{10}$ aryl, unsubstituted or substituted 5 or 6 membered heterocyclyl comprising 1 or 2 hetero atoms selected from N, O and S, $C_1\text{-}C_8$ alkoxy, halo $C_1\text{-}C_8$ alkoxy, $C_5\text{-}C_{10}$ aryloxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocyclyl $C_1\text{-}C_8$ alkoxy, unsubstituted or substituted amino, halogen, unsubstituted or substituted sulfamoyl, or nitro; and

R^{10} is $C_1\text{-}C_8$ alkyl, halo $C_1\text{-}C_8$ alkyl, $C_1\text{-}C_8$ alkoxy, unsubstituted or substituted heterocyclyl $C_1\text{-}C_8$ alkoxy, unsubstituted or substituted amino, or halogen; or each pair of adjacent substituents R^7 and R^8 , or R^8 and R^9 or R^9 and R^{10} , is $-\text{NH-CH=CH-}$, $-\text{CH=CH-NH-}$, $-\text{NH-N=CH-}$, $-\text{CH=N-NH-}$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2^-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2^-$, $-\text{O-CH}_2\text{-O-}$, or $-\text{O-CF}_2\text{-O-}$;

A is C or N.

4. A compound of formula I according to claim 1, wherein

each of R^0 or R^2 independently is hydrogen, piperazino, N-methylpiperazino or 1-methyl-4-piperidyloxy;

R^1 is hydrogen, piperazino, N-methylpiperazino, morpholino, 1-methyl-4-piperidinyloxy, 3-morpholinopropoxy or 2-morpholinoethoxy;

R^3 is sulfamoyl, methylsulfamoyl or propylsulfamoyl; or

the pair of adjacent substituents R^0 and R^1 , or R^1 and R^2 is $-\text{O-CH}_2\text{-O-}$, or the pair of adjacent substituents R^2 and R^3 is $-\text{CH}_2\text{-NH-CO-}$ or $-\text{CH}_2\text{-NH-SO}_2^-$;

R⁴ is hydrogen;

R⁵ is hydrogen, chloro, bromo, trifluoromethyl or nitro;

R⁶ is hydrogen;

each of R⁷ and R⁹ independently is hydrogen, C₁-C₈alkyl, haloC₁-C₈alkyl, unsubstituted or substituted C₅-C₁₀aryl, unsubstituted or substituted 5 or 6 membered heterocycll comprising 1 or 2 hetero atoms selected from N, O and S, C₁-C₈alkoxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocycllC₁-C₈alkoxy, unsubstituted or substituted amino, halogen, unsubstituted or substituted carbamoyl, or unsubstituted or substituted sulfamoyl;

R⁸ is hydrogen, C₁-C₈alkyl, haloC₁-C₈alkyl, C₅-C₁₀aryl, unsubstituted or substituted 5 or 6 membered heterocycll comprising 1 or 2 hetero atoms selected from N, O and S, C₁-C₈alkoxy, haloC₁-C₈alkoxy, C₅-C₁₀aryloxy, unsubstituted or substituted heterocyclyloxy, unsubstituted or substituted heterocycllC₁-C₈alkoxy, unsubstituted or substituted amino, halogen, unsubstituted or substituted sulfamoyl, or nitro; and

R¹⁰ is C₁-C₈alkyl, haloC₁-C₈alkyl, C₁-C₈alkoxy, unsubstituted or substituted heterocycllC₁-C₈alkoxy, unsubstituted or substituted amino, or halogen; or each pair of adjacent substituents R⁷ and R⁸, or R⁸ and R⁹ or R⁹ and R¹⁰, is -NH-CH=CH-, -CH=CH-NH-, -NH-N=CH-, -CH=N-NH-, -CH₂-CH₂-CH₂-, -CH₂-CH₂-CH₂-CH₂-, -O-CH₂-O-, or -O-CF₂-O-;

A is C or N.

5. A compound of formula I according to claim 1, wherein

each of R⁰ or R² independently is hydrogen, piperazino, N-methylpiperazino or 1-methyl-4-piperidyloxy;

R¹ is hydrogen, piperazino, N-methylpiperazino, morpholino, 1-methyl-4-piperidinyloxy, 3-morpholinopropoxy or 2-morpholinoethoxy;

R³ is sulfamoyl, methylsulfamoyl or propylsulfamoyl; or

the pair of adjacent substituents R⁰ and R¹, or R¹ and R² is -O-CH₂-O-, or the pair of adjacent substituents R² and R³ is -CH₂-NH-CO- or -CH₂-NH-SO₂-;

R⁴ is hydrogen;

R⁵ is hydrogen, chloro, bromo, trifluoromethyl or nitro;

R⁶ is hydrogen;

each of R⁷ and R⁹ independently is hydrogen, methyl, isopropyl, trifluoromethyl, phenyl, o-, m- or p-methoxyphenyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy,

ethoxy, isopropoxy, phenoxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 2-(1-imidazolyl)ethoxy, dimethylamino, fluoro, morpholinocarbonyl, piperidinocarbonyl, piperazinocarbonyl or cyclohexylcarbamoyl;

R⁸ is hydrogen, methyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, trifluoromethoxy, phenoxy, 1-methyl-4-piperidyloxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 3-(N-methylpiperazino)-propoxy, methylamino, fluoro, chloro, sulfamoyl or nitro; and

R¹⁰ is methyl, butyl, methoxy, ethoxy, 2-(1-imidazolyl)ethoxy, methylamino, dimethylamino or fluoro; or

the pair of adjacent substituents R⁷ and R⁸ or R⁸ and R⁹ is -O-CH₂-O- or the pair of adjacent substituents R⁹ and R¹⁰ is -NH-CH=CH-, -CH=N-NH-, -CH₂-CH₂-CH₂-, -CH₂-CH₂-CH₂-CH₂- or -O-CF₂-O-;

A is C or N.

6. A compound of formula I according to claim 1, wherein

each of R⁰, R¹ or R² is hydrogen;

R³ is sulfamoyl, methylsulfamoyl or propylsulfamoyl;

R⁴ is hydrogen;

R⁵ is chloro or bromo;

R⁶ is hydrogen;

each of R⁷ and R⁹ independently is hydrogen, methyl, isopropyl, trifluoromethyl, phenyl, o-, m- or p-methoxyphenyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, isopropoxy, phenoxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 2-(1-imidazolyl)ethoxy, dimethylamino, fluoro, morpholinocarbonyl, piperidinocarbonyl, piperazinocarbonyl or cyclohexylcarbamoyl;

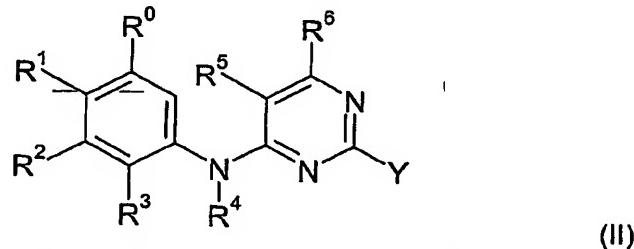
R⁸ is hydrogen, methyl, piperidino, piperazino, N-methylpiperazino, morpholino, methoxy, ethoxy, trifluoromethoxy, phenoxy, 1-methyl-4-piperidyloxy, 3-morpholinopropoxy, 2-morpholinoethoxy, 3-(N-methylpiperazino)-propoxy, methylamino, fluoro, chloro, sulfamoyl or nitro; and

R¹⁰ is methyl, butyl, methoxy, ethoxy, 2-(1-imidazolyl)ethoxy, methylamino, dimethylamino or fluoro; or

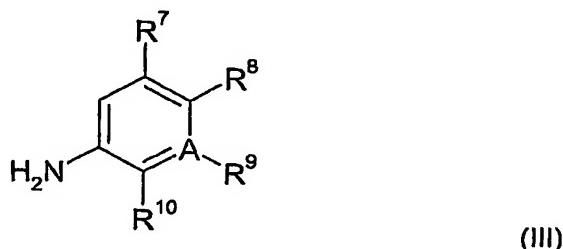
the pair of adjacent substituents R⁷ and R⁸ or R⁸ and R⁹ is -O-CH₂-O-, or the pair of adjacent substituents R⁹ and R¹⁰ is -NH-CH=CH-, -CH=N-NH-, -CH₂-CH₂-CH₂-, -CH₂-CH₂-CH₂-CH₂- or -O-CF₂-O-;

A is C or N.

7. The compound of formula I according to claim 1, wherein each of R⁰, R¹ or R² is hydrogen, R³ is methylsulfamoyl, R⁴ is hydrogen, R⁵ is bromo, R⁶ is hydrogen, each of R⁷ and R⁸ is methoxy, R⁹ is hydrogen, and R¹⁰ is methyl, and A is C or N.
8. The compound of formula I according to claim 1, wherein each of R⁰, R¹ or R² is hydrogen, R³ is methylsulfamoyl, R⁴ is hydrogen, R⁵ is bromo, R⁶ is hydrogen, each of R⁷ and R⁸ is hydrogen, and the pair of adjacent substituents R⁹ and R¹⁰ is -CH₂-CH₂-CH₂-, and A is C or N.
9. The compound of formula 2-[5-Chloro-2-[4-(3-methylamino-pyrrolidin-1-yl)-phenylamino]-pyrimidin-4-ylamino]-N-Isopropyl-benzenesulfonamide.
10. A process for the production of a compound of formula I according to claim 1, comprising reacting a compound of formula II



wherein R⁰, R¹, R², R³, R⁴, R⁵, and R⁶ are as defined in claim 1, and Y is a leaving group, with a compound of formula III



wherein R⁷, R⁸, R⁹ and R¹⁰ are as defined in claim 1;

and, if desired, converting a compound of formula I, wherein the substituents have the meaning as defined in claim 1, into another compound of formula I as defined in claim 1;

and recovering the resulting compound of formula I in free form or as a salt, and, when required, converting the compound of formula I obtained in free form into the desired salt, or an obtained salt into the free form.

11. A pharmaceutical composition comprising a compound according to any one of claims 1 to 9, as active ingredient together with one or more pharmaceutically acceptable diluents or carriers.
12. The use of a compound according to any one of claims 1 to 9 for the manufacture of a medicament for the treatment or prevention of neoplastic diseases and immune system disorders.
13. A combination comprising a therapeutically effective amount a compound according to any one of claims 1 to 9 and one or more further drug substances, said further drug substance being useful in the treatment of neoplastic diseases or immune system disorders.
14. A method for the treatment of neoplastic diseases and immune system disorders in a subject in need thereof which comprises administering an effective amount of a compound according to any one of claims 1 to 9 or a pharmaceutical composition comprising same.
15. Use of a compound according to any one of claims 1 to 9 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of a disease which responds to inhibition of focal adhesion kinase or/and IGF-1 Receptor.
16. The use according to claim 15, wherein the disease to be treated is selected from proliferative disease .
17. The use according to claim 16, wherein the proliferative disease to be treated is selected from a tumor of, breast, renal , prostate, colorectal, thyroid, ovarian, pancreas, neuronal, lung, uterine and gastro-intestinal tumours as well as osteosarcomas and melanomas.
18. The use according to claim 15, wherein the disease to be treated is an immune disease.

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19. Use of a compound according to any one of claims 1 to 9 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of inflammatory and/or an immune disorder.
20. Use according to claim 19 wherein the inflammatory and/or immune disorder is selected from transplant rejection, allergy and autoimmune disorders mediated by immune cells including T lymphocytes, B lymphocytes, macrophages, dendritic cells, mast cells and eosinophils.
21. The use according to any one of claims 14 to 19, wherein the compound is 2-[5-Bromo-2-(2-methoxy-5-morpholin-4-yl-phenylamino)-pyrimidin-4-ylamino]-N-methyl-benzenesulfonamide or a pharmaceutically acceptable salt thereof.
22. The use according to any one of claims 14 to 19, wherein the compound is selected from 2-[5-chloro-2-(2-methoxy-4-morpholin-4-yl-phenylamino)-pyrimidin-4-ylamino]-N-methyl-benzamide, N²-(4-[1,4]Bipiperidinyl-1'-yl-2-methoxy-phenyl)-5-chloro-N⁴-[2-(propane-1-sulfonyl)-phenyl]-pyrimidine-2,4-diamine and 2-[5-Chloro-2-[2-methoxy-4-(4-methyl-piperazin-1-yl)-phenylamino]-pyrimidin-4-ylamino]-N-isopropyl-benzenesulfonamide, or a pharmaceutically acceptable salt thereof.